

Application No.: 09/04,464
Docket No.: BB1193 USDIV

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REMARKS

Reconsideration and allowance are respectfully requested.

Claims 31-43 are now pending, with Claim 31 being the sole independent claim.

Claims 1-30 have been cancelled and Claims 44-66 have been withdrawn without prejudice to or disclaimer of the subject matter recited therein.

Claims 31 and 37-43 have been amended. No new matter has been added.

Turning now to the Office Action mailed November 28, 2003:

Enclosed herewith is a copy of the previously submitted Information Disclosure Statement, the certificate of mailing dated June 15, 2001, and a copy of the postcard date stamped by the U.S. Patent and Trademark Office as being received on June 18, 2001, that were submitted in connection with the above-identified application.

These papers are being resubmitted, since the original papers appear to be missing. Applicants respectfully request entry of these papers with an effective date of June 15, 2001.

Regarding the oath or declaration, Applicants respectfully traverse. Applicants submit that the statutes and rules do not require a date of execution of the declaration. Please see MPEP 602.05 (Oath or Declaration - Date of Execution). See also 35 U.S.C. 115 and 37 CFR 1.63.

Applicants have amended both the title, the abstract and Claim 31 as suggested by the Examiner. Regarding the Section 112, second paragraph rejection, Applicants have amended Claims 37-43 as suggested by the Examiner. No new matter has been added by these amendments. In light of the amendments, withdrawal of these objections/rejections is kindly requested.

Regarding the Section 112, first paragraph enablement rejection, Applicants respectfully traverse.

Applicants submit that the specification enables a person of ordinary skill to make and use the claimed invention commensurate in scope with the pending claims.

Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence having 80% sequence identity to SEQ ID NO:10 while still retaining lysyl-tRNA synthetase activity.

Applicants believe the following three articles to be well-known to one of ordinary skill in the art:

1. Arnez et al. (*TIBS* 22:211-216 (1997)), entitled "Structural and functional consideration of the aminocacylation reaction" ("Arnez"; cited in a Supplemental IDS filed simultaneously herewith);
2. Desogus et al. (*Biochem.* 39:8418-8425 (2000)), entitled "Active Site of

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("Desogus"; cited in a Supplemental IDS filed simultaneously herewith);
and

3. Girtch et al., (*Eur. J. Biochem.* 244:310-317 (1997)), entitled "A root specific iron-regulated gene of tomato encodes a lysyl-tRNA-synthetase-like protein" ("Girtch", cited by the Examiner).

Arnez discusses the common and distinguishing structural and functional themes of the twenty known aminoacyl-tRNA synthetases and lists in Table 1, on page 212, the three conserved motifs for class II tRNA synthetases. Motif 1 contains an absolutely conserved proline, and motifs 2 and 3 contain an invariant arginine. Desogus shows in Figure 5, on page 8424, a partial alignment of selected class II aminoacyl-tRNA synthetases. The invariant arginines and other residues which are important for substrate binding are indicated by asterisks. Girtch shows in Figure 1, on pages 312-313, a complete amino acid sequence of the tomato lysyl-tRNA synthetase with corresponding sequences from other species. The three highly conserved motifs (1, 2 and 3) are underlined.

Appendix A, attached hereto, is a sequence alignment of the following three lysyl-tRNA synthetases:

1. SEQ ID NO:10 of the pending claims (maize lysyl-tRNA synthetase);
2. sequence encoding GenBank Accession Number AF125574; equivalent to NCBI GI 4325324 (*Arabidopsis thaliana* lysyl-tRNA synthetase cited in the instant application); and
3. sequence encoding GenBank Accession Number X94451 (*Lycopersicon esculentum* lysyl-tRNA synthetase cited by the Examiner).

The conserved amino acids among all three sequences can be found in Consensus #1. The three conserved motifs indicative of class II aminoacyl-tRNA synthetases are present and indicated by boxes. The absolutely conserved proline and invariant arginines are present in SEQ ID NO:10 and marked with asterisks.

Attached as Appendix B is a chart setting forth a comparison of the percent identity (and percent divergence in the lower half triangle), using the Clustal alignment method recited in the pending claims, between the three lysyl-tRNA synthetases found in Appendix A.

Applicants submit that there is a well-known correlation between the lysyl-tRNA synthetase activity disclosed and claimed in the instant specification and lysyl-tRNA synthetase protein (and corresponding nucleic acid) structure, based on the remarks above and the conserved structural features.

Given this known correlation between lysyl-tRNA synthetase activity and protein structure, Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence

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having 80% sequence identity to SEQ ID NO:10 while still retaining lysyl-tRNA synthetase activity.

The experimentation necessary to make the claimed invention to the full extent of its scope is not undue in this field, where the level of skill is very high. For example, Applicants disclose methods for expressing the recombinant constructs in monocot, dicot and microbial cells (see Examples 7-9 on pages 22-26). With the expressed polypeptide, activity may be determined using routine tests, such as those presented by Zon et al. (see page 28, lines 4-6 of the instant specification).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of the claims under 35 USC §112, first paragraph enablement rejection.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

Please charge any fees or credit any overpayment of fees which are required in connection herewith to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Applicants' undersigned may be reached at the below-listed numbers.

Respectfully submitted,

Dawn S. Clark

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Dated: May 25, 2004

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Appendix A

Consensus #1

BB1193DIVSeqIdNo10

GI 4325324

GenBank X94451

```
.....10.....20.....30.....40.....50.....60.....
LSLHLLRVSPSPSPSRPLNNEALVSRDM SGLEEK - GL TG QN PPAGEGGE 59
--GAADQTTKALSBL MDSSTT NAE SA AG R - - - - 37
--SSVST 8
```

Consensus #1

BB1193DIVSeqIdNo10

GI 4325324

GenBank X94451

```
...SKNA.K.E.K.K..E.....B...KA.....D.TQY..NR
.....70.....80.....90.....100.....110.....120.....
--K K E R K L R L E - - - - - SGKP S 118
--K Q M Q K R D A E K Q P A S S V E E A 94
--K K A E Q L - - - - - ROMEQHNLPEN L L A 61
```

Consensus #1

BB1193DIVSeqIdNo10

GI 4325324

GenBank X94451

```
L.....G.NPYPHKF....S.P.I..Y..L..G.....LAGR...KR.SSS
.....130.....140.....150.....160.....170.....180.....
--A D I T V P G I V K R T S E K L T V A C N T 178
--Y A A E K E S K T G S N N D H V N A B S S 154
--RNIE RES I F I T F S R A H T F F P I D M C V I A 121
```

Appendix A

Consensus #1

99B1193DIVSeqIdNo10

FI 4325324

GenBank X94451

Conclusion #1

BB1193DIVSeqIdNo10

GI 4325324

GenBank X94451

Consensus #1

BB1193DIVseqIdNo10

GI 4325324

GenBank X94451

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Appendix A

motif 2

Consensus #1

BB1193DIVSeqIdNo10
GI 4325324
GenBank X94451

Consensus #1

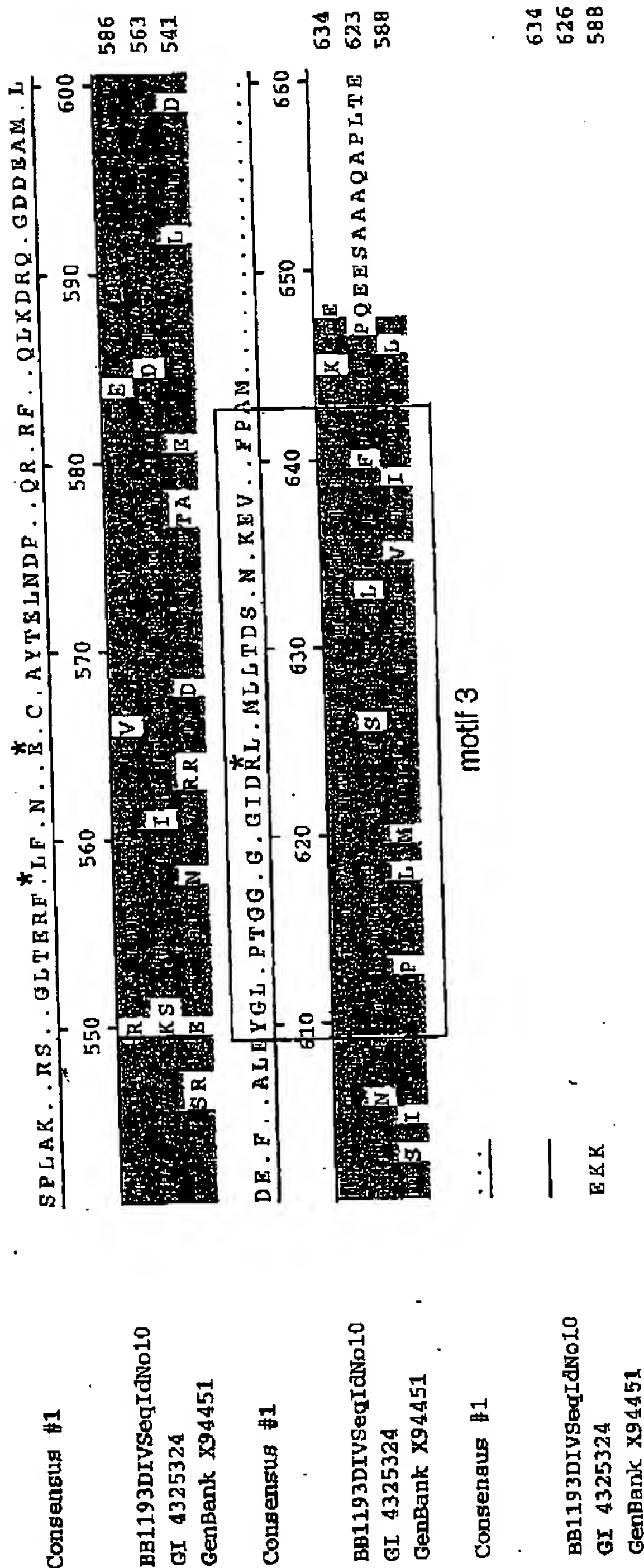
BB1193DIVSeqIdNo10
GI 4325324
GenBank X94451

Consensus #1

BB1193DIVSeqIdNo10
GI 4325324
GenBank X94451

N.L...L..R...PELYLK..L.VGG
 .RVYE.GK.FRNEG.DLTH.*
 .PET.CE.YMA.ADY
 370 380 390 400 410 420
 406
 383
 361
 NDLM..TB..LSGMVK.LTG.YKI.Y.ANG...PIBIDFTPPFR.I.M...LE...A...
 430 440 450 460 470 480
 466
 443
 421
 IP.DL..S..AN..L...C...DVKCPPP.TT.RLLDKLVG.F.E..C.NPTFIIN.PEIM
 490 500 510 520 530 540
 526
 503
 481

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Consensus #1: When all match the residue on the Consensus show the residue of the Consensus, otherwise show ‘.’

Shade (with black at 40% fill) residues that match the Consensus named "Consensus #1" exactly.

The three highly conserved motifs (1, 2 and 3) are indicated by boxes. Residues which are important for substrate binding are indicated by asterisks.

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Appendix B

Percent Identity

	1	2	3	
1		67.7	64.5	1
2	36.0		60.2	2
3	43.4	50.1		3
	1	2	3	

Divergence

BB1193DIVSeqIdNo10
NCBI GI 4325324
GenBank X94451